

§Appl. No. 09/856,044  
Amdt. dated February 3, 2005  
Reply to Office Action of, November 3, 2004

### **REMARKS**

Support for claim 16 can be found through the specification, e.g., Page 9, lines 30-33 and Page 11, lines 304.

### **Rejections under §103**

It is alleged in the Office action on Page 3 that it would have been obvious to combine Mann et al. (*Biol. Mass Spec.*, 22:338-345, 1993) and Yates (U.S. Pat. No. 5,538,897). It is stated that: "Mann et al. state a desire for a more accurate method of matching protein samples to organisms (p. 340 column 2-p. 341 column 1). Yates et al. provides such a technique."

As already argued in the Response filed August 11, 2004, there is no disclosure or suggestion in Yates of using intact, undigested proteins. Yates expressly states: "It is believed that the present invention can be used with any size peptide. The process **requires** that peptides be fragmented and there are methods for achieving fragmentation of very large proteins." (Emphasis added.) Column 18, lines 57-60. The disclosures on Column 4 (lines 15-25 and 49-65) of the Yates patent (as cited in the Office action) refers to the fact that peptides are derived from a protein, but do not disclose the use of intact, undigested proteins for identification purposes. This is clear from the later disclosure on Column 18 (see above) that requires the utilization of peptide fragments. Thus, the Yates "technique" referred to in the Office action (see above) is to extract information from peptide fragments derived from an intact protein. This is stated explicitly in the **Summary of the Invention**: "According to the present invention, known amino acid sequences, e.g., in a protein sequence library, are used to calculate or predict one or more candidate fragment spectra. The predicted fragment spectra are then compared with an experimentally-derived fragment spectrum to determine the best match or matches." Yates, Column 1, line 65-Column 2, line 3." This is echoed throughout the disclosure. See, e.g., Column 17, lines 47-57, where Yates describes digesting the proteins to create peptide

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fragments. Combining Mann et al. with Yates, therefore, would not have led the skilled worker to the claimed invention since using intact protein would defeat the purpose of Yates.

Mann et al., describe using isolated proteins, not a sample comprising a plurality of proteins. There is no example of using other than an isolated protein, and it is expressly stated in the “Conclusions and Prospects” on Page 343: “With the present capabilities of mass spectrometers molecular weight measurement is a natural first step in the characterization of an **isolated** protein.” (Emphasis added.) Moreover, Mann et al. describe various difficulties of using intact protein mass, and suggest using proteolytic derived fragments, instead. “These possible sources of error limit the generality of the search by intact protein mass. Furthermore, it is often not easy to purify large proteins sufficiently to get an accurate molecular weight. Therefore, we have investigated another, more error-tolerant way of matching proteins against a database.” This suggestion is to search by molecular weights of proteolytically derived peptide. See, Page 341, 1<sup>st</sup> column. This even more so, when combined with Yates as suggested in the Office action, would have led the skilled worker away from using intact proteins.

The combination of Wang et al. (Rapid Communication in Mass Spectrometry, 1998) and Yates also would not have led the skilled worker to the claimed invention. Two arguments were presented in the Office action on Page 4 to rebut Applicant’s position that the claims were not obvious. Neither are correct.

“First, Yates et al. disclose that there is no theoretical or practical limit to the size of the proteins used in his method (column 19). Yates et al. has experimentally used proteins of up to 26 residues (column 19). Yates et al. could perform his method on small proteins such as cyclotides.”

It is true that Yates believes that any size peptide can be used in his technique. (“It is believed that the present invention can be used with any size peptide.” Column 18, lines 57-58.) However, the very next sentence (from the same paragraph on Column 19 quoted by the examiner) states: “The process requires that peptides be fragmented ....” The examiner has not

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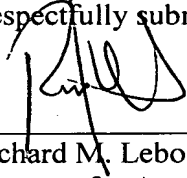
presented any evidence or reasoning that would have motivated the skilled worker to utilize intact, undigested proteins in place of fragments. This would be completely contrary to the teachings in Yates whose disclosure is restricted to fragments.

In the examiner's second argument, it is alleged that "Second, the claims as written do not require any particular input order to search for intact proteins. As the claim is written, a user may input sequences of the full protein or of only a fragment of a full protein." (Emphasis added.) To the contrary, claim 13 expressly recites "searching a database for the molecular weights of a plurality of intact, undigested proteins ..." Therefore, the statement that fragments or full proteins maybe searched is incorrect, since the search for intact, undigested proteins is not provided in the alternative.

In view of the above remarks, favorable reconsideration is courteously requested. If there are any remaining issues which could be expedited by a telephone conference, the Examiner is courteously invited to telephone counsel at the number indicated below.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,



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